

Supplemental Table 4. ICU day 3 plasma proteins that predict COVID19 outcome.

Num	Assay	Uniprot ID	Function
1.	IL12RB1	P42701	One of the two subunits that form the IL-12 receptor (1). Expressed primarily on activated T cells and NK cells, less so on dendritic cells and some B-cells (1, 2). This subunit is also shared with the IL-23 receptor (3).
2.	CLM-1	Q8TDQ1	CMRF35-like molecule 1 also called CD300f, is a receptor for phosphatidylserine presented on the outer membrane of apoptotic cells (4), that promotes macrophage and inhibits DC efferocytosis (5).
3.	CXCL9	Q07325	A chemokine produced by airway epithelial cells in response to infection (6), also induced by IFN γ and in endothelial cells by TNF (7). An agonist for CXCR3 on T cells and natural killer cells (7). Promotes NK, Th1, monocyte, DC, neutrophil, and eosinophil recruitment (6).
4.	FAM3B	P58499	Family with sequence similarity 3, also called pancreatic derived factor (PANDER), is a cytokine-like protein that is highly expressed in pancreatic islets and high serum levels are associated with the progression of metabolic syndrome and type 2 diabetes (8).
5.	OPTC	Q9UBM4	Opticin is an extracellular matrix protein associated with collagen in the vitreous humor where it binds heparan and chondroitin sulfate (9, 10). It is an anti-angiogenic factor in retinas (10).
6.	THY 1	P04216	Thymocyte differentiation antigen 1 is a glycoprotein expressed on the outer surface of many cell types including fibroblasts, T cells and activated endothelial cells and has a soluble form (11). Its function is cell and tissue-dependent, but is pro-fibrotic in pulmonary fibroblasts in pulmonary fibrosis (11).
7.	ICOSLG	O75144	Inducible costimulator ligand is a transmembrane protein expressed by B cells, monocytes, DCs T cells and endothelial cells; TNF α is required for induction (12). It activates the inducible costimulator in the thymus and on activated T cells (12).
8.	IGF1R	P08069	A tyrosine kinase receptor expressed on T and B cells, macrophages, NK cells and granulocytes where its ligands, insulin-like growth factor 1 and 2, causes various effects such as proliferation, cytokine production and priming/activation (7).
9.	IL10.1	P22301	An important anti-inflammatory cytokine, expressed in virtually all immune cells except plasmacytoid DCs, it works to limit immune responses and prevent host damage (13).

10.	CLMP	Q9H6B4	Coxsackievirus and adenovirus receptor-like membrane protein is a transmembrane glycoprotein involved in homophilic cell-cell adhesion and is expressed in a wide variety of tissues (14).
11.	IL10	P22301	See “IL10.1” above.
12.	CD83	Q01151	Expressed on B and T cells, monocytes, DCs, microglia and neutrophils, and has soluble and membrane-bound forms (15). Membrane-bound CD83 is essential for CD4 ⁺ T cell development and inhibiting autoimmunity, soluble CD83 induces regulatory mechanisms for tolerance (15).
13.	ROR1	Q01973	A transmembrane receptor tyrosine kinase that is activated by Wnt family ligands and is mainly thought to be involved in organ/tissue genesis during development (16). Though recent evidence suggests it may be involved in pro-inflammatory p65 activation, at least in cancer (17).
14.	PVRL4	Q96NY8	Poliovirus receptor-related protein 4 also called nectin-4 is a cell-cell adhesion molecule in adherens junctions, overexpressed in several cancers (18).
15.	IL32	P24001	Expressed by PBMCs, epithelial cells and NKs, it up-regulates other pro-inflammatory cytokines and has several isoforms (19). Airway epithelial cell production is increased by viral infections and oxidative stress (6).
16.	CA12	O43570	Carbonic anhydrase 12 is membrane-associated glycoprotein that catalyzes the reversible hydration of carbon dioxide (20). CA12 is up-regulated by hypoxia, at least in tumor environments (21) and CA activity is associated with sleep apnea-related hypoxemia (22).
17.	NCS1	P62166	Neuronal calcium sensor 1 is a cytosolic protein involved in several cellular functions through binding partners and intracellular Ca ²⁺ regulation (23). It is highly expressed in neurons, but is not neuron-specific (23).
18.	FLRT2	O43155	Fibronectin leucine rich transmembrane protein 2 was first discovered in a screen for extracellular matrix proteins (24) and participates in homotypic cell-cell adhesion as well as fibroblast growth factor receptor signaling (25).
19.	S100A11	P31949	A cytosolic calcium-binding protein of the S100 family, it is involved in growth arrest in contact inhibition (26). It is expressed in a wide variety of cells and is secreted by an unconventional pathway (26). It is involved in cell-cell contacts and can promote cell migration in response to hypoxia-induced mitogenic factor (27).
20.	TOP2B	Q02880	DNA topoisomerase II beta is expressed in a wide variety of tissues and throughout the cell cycle (28). Mostly found in the cell’s nucleus, it is one of the enzymes that catalyzes topological changes in DNA (28).

21.	ANGPTL7	O43827	Angiopoietin-like protein 7 is an orphan ligand, but appears to be involved in hematopoietic stem cell regulation and self-renewal (29). Its serum concentration is higher in obese subjects compared to non-obese controls and can be lowered with exercise (30).
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CD – cluster of differentiation

CXCL – CXC ligand

CXCR – CXC receptor

DC – dendritic cell

IFN γ – interferon gamma

IL – interleukin

NK – natural killer cell

PBMC – peripheral blood monocyte cell

STAT – signal transducer and activator of transcription

Th# – type # T helper cell

TNF α – tumor necrosis factor alpha

References

1. Presky DH, Yang H, Minetti LJ, et al.: A functional interleukin 12 receptor complex is composed of two β -type cytokine receptor subunits. *PNAS* 1996; 93:14002–14007
2. Trinchieri G: Interleukin-12 and the regulation of innate resistance and adaptive immunity. *Nature Reviews Immunology* 2003; 3:133–146
3. Wojno EDT, Hunter CA, Stumhofer JS: The immunobiology of the Interleukin-12 family: Room for discovery. *Immunity* 2019; 50:851–870
4. Choi S-C, Simhadri VR, Tian L, et al.: Cutting Edge: Mouse CD300f (CLM-1) recognizes outer-membrane exposed phosphatidylserine and can promote phagocytosis. *J Immunol* 2011; 187:3483–3487
5. Tian L, Choi S-C, Lee H-N, et al.: Enhanced efferocytosis by dendritic cells underlies memory T-cell expansion and susceptibility to autoimmune disease in CD300f-deficient mice. *Cell Death Differ* 2016; 23:1086–1096

6. Foti M, Locati M: Cytokine Effector Functions in Tissues [Internet]. San Diego, UNITED STATES: Elsevier Science & Technology; 2017. [cited 2020 Jun 9] Available from: <http://ebookcentral.proquest.com/lib/west/detail.action?docID=4917635>
7. Thomson AW, Lotze MT: The cytokine handbook. Amsterdam; Boston: Academic Press; 2003.
8. Zhang X, Yang W, Wang J, et al.: FAM3 gene family: A promising therapeutical target for NAFLD and type 2 diabetes. *Metabolism* 2018; 81:71–82
9. Le Goff MM, Bishop PN: Focus on Molecules: Opticin. *Experimental Eye Research* 2007; 85:303–304
10. Bishop PN: The role of extracellular matrix in retinal vascular development and preretinal neovascularization. *Experimental Eye Research* 2015; 133:30–36
11. Bradley JA, Ramirez G, Hagood JS: Roles and Regulation of Thy-1, a Context-Dependent Modulator of Cell Phenotype. *Biofactors* 2009; 35:258–265
12. Richter G, Burdach S: ICOS: A New Costimulatory Ligand/Receptor Pair and Its Role in T-Cell Activation. *ORT* 2004; 27:91–95
13. Howes A, Stimpson P, Redford P, et al.: Interleukin-10: Cytokines in Anti-inflammation and Tolerance [Internet]. In: Yoshimoto T, Yoshimoto T, editor(s). *Cytokine Frontiers: Regulation of Immune Responses in Health and Disease*. Tokyo: Springer Japan; 2014. p. 327–352.[cited 2020 Jun 9] Available from: https://doi.org/10.1007/978-4-431-54442-5_13
14. Matthäus C, Langhorst H, Schütz L, et al.: Cell-cell communication mediated by the CAR subgroup of immunoglobulin cell adhesion molecules in health and disease. *Molecular and Cellular Neuroscience* 2017; 81:32–40
15. Grosche L, Knippertz I, König C, et al.: The CD83 Molecule – An Important Immune Checkpoint [Internet]. *Front Immunol* 2020; 11[cited 2020 Jun 10] Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7181454/>
16. Stricker S, Rauschenberger V, Schambony A: Chapter Four - ROR-Family Receptor Tyrosine Kinases [Internet]. In: Jenny A, editor(s). *Current Topics in Developmental Biology*. Academic Press; 2017. p. 105–142.[cited 2020 Jun 10] Available from: <http://www.sciencedirect.com/science/article/pii/S007021531630179X>
17. Lopez-Bergami P, Barbero G: The emerging role of Wnt5a in the promotion of a pro-inflammatory and immunosuppressive tumor microenvironment. *Cancer Metastasis Rev* 2020;
18. Takai Y, Miyoshi J, Ikeda W, et al.: Nectins and nectin-like molecules: roles in contact inhibition of cell movement and proliferation. *Nat Rev Mol Cell Biol* 2008; 9:603–615

19. Catalan-Dibene J, McIntyre LL, Zlotnik A: Interleukin 30 to Interleukin 40. *Journal of Interferon & Cytokine Research* 2018; 38:423
20. Waheed A, Sly WS, Doisy EA: Carbonic Anhydrase XII Functions in Health and Disease. *Gene* 2017; 623:33–40
21. Chiche J, Ilc K, Laferrière J, et al.: Hypoxia-Inducible Carbonic Anhydrase IX and XII Promote Tumor Cell Growth by Counteracting Acidosis through the Regulation of the Intracellular pH. *Cancer Res* 2009; 69:358–368
22. Wang T, Eskandari D, Zou D, et al.: Increased Carbonic Anhydrase Activity is Associated with Sleep Apnea Severity and Related Hypoxemia. *Sleep* 2015; 38:1067–1073
23. Boeckel GR, Ehrlich BE: NCS-1 is a Regulator of Calcium Signaling in Health and Disease. *Biochim Biophys Acta Mol Cell Res* 2018; 1865:1660–1667
24. Lacy SE, Bönnemann CG, Buzney EA, et al.: Identification of FLRT1, FLRT2, and FLRT3: A Novel Family of Transmembrane Leucine-Rich Repeat Proteins. *Genomics* 1999; 62:417–426
25. Karaulanov EE, Böttcher RT, Niehrs C: A role for fibronectin-leucine-rich transmembrane cell-surface proteins in homotypic cell adhesion. *EMBO Rep* 2006; 7:283–290
26. Sakaguchi M, Huh N: S100A11, a dual growth regulator of epidermal keratinocytes. *Amino Acids* 2011; 41:797–807
27. Gross SR, Sin CGT, Barraclough R, et al.: Joining S100 proteins and migration: for better or for worse, in sickness and in health. *Cell Mol Life Sci* 2014; 71:1551–1579
28. Austin CA, Lee KC, Swan RL, et al.: TOP2B: The First Thirty Years [Internet]. *Int J Mol Sci* 2018; 19[cited 2020 Jun 11] Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6163646/>
29. Kadomatsu T, Oike Y: Roles of angiopoietin-like proteins in regulation of stem cell activity. *J Biochem* 2019; 165:309–315
30. Abu-Farha M, Cherian P, Al-Khairi I, et al.: Plasma and adipose tissue level of angiopoietin-like 7 (ANGPTL7) are increased in obesity and reduced after physical exercise. *PLOS ONE* 2017; 12:e0173024